AMENDMENTS TO THE CLAIMS:

1. (Canceled)

2. (Previously Amended) The method of claim 6, wherein the marker that reflects the activity of osteoblasts is:

(1) a marker associated with the phase of osteoblast proliferation and matrix formation and a marker associated with the phase of calcification; or

(2) a marker associated with the phase of matrix maturation and a marker associated with the phase of calcification.

3. (Previously Amended) The method according to claim 6, wherein the marker that reflects the activity of osteoblasts is:

(1) Carboxyterminal propeptide of type I procollagen or Amino terminal propeptide of type I procollagen and osteocalcin; or

(2) Bone specific alkaliphosphatase and osteocalcin.

4. (Previously amended) The method according to claim 6, wherein the marker that reflects the action of osteoclasts is a marker associated with bone type I collagen.

5. (Previously amended) The method according to claim 6, wherein the marker that reflects the action of

osteoclasts is deoxypyridinoline and/or Carboxyterminal telopeptide of type I collagen.

6. (Currently Amended) A method of diagnosing metastasis of malignant tumor to bone using two markers comprising both a first marker that reflects the activity of osteoblasts and a second marker that reflects the action of osteoclasts,

~~based on the value of a crossover index or the ratio between a marker associated with the phase of osteoblast proliferation and matrix formation and the measured value of the marker that reflects the action of osteoclasts, or on the value of a crossover index or the ratio between a marker associated with the phase of calcification and a marker associated with the phase of matrix maturation and the measured value of a marker associated with bone type I collagen,~~

~~whereby~~ wherein ~~,~~ the amelioration of bone metastasis or therapeutic effect and the degree of the exacerbation of bone metastasis are diagnosed ~~correctly~~ by monitoring said two markers, ~~one~~ said first marker being associated with osteoblasts and targeted to evaluation of therapeutic effect, and ~~the other~~ said second marker being associated with osteoclasts and targeted to evaluation of worsening of the disease.

7. (Canceled)

8. (Previously amended) A method of evaluating the therapeutic efficacy of a drug using a marker that reflects the activity of osteoblasts and a marker that reflects the action of osteoclasts, whereby the amelioration of bone metastasis or therapeutic effect and the degree of the exacerbation of bone metastasis are diagnosed correctly by monitoring said two markers, one associated with osteoblasts and targeted to evaluation of therapeutic effect, and the other associated with osteoclasts and targeted to evaluation of worsening of the disease.

9. (Original) The method according to claim 8, wherein the drug is a cancer control therapeutic agent.

10. (Original) The method according to claim 8, wherein the drug is a bone resorption suppressant.

11. (Original) The method according to claim 8, wherein the drug is an endocrine therapeutic agent.

12. (Previously Amended) The method according to claim 8, wherein the marker that reflects the activity of osteoblasts is:

(1) a marker associated with the phase of osteoblast proliferation and matrix formation and a marker associated with the phase of calcification; or

(2) a marker associated with the phase of matrix maturation and a marker associated with the phase of calcification.

13. (Previously Amended) The method according to claim 8, wherein the marker that reflects the activity of osteoblasts is:

(1) Carboxyterminal propeptide of type I procollagen or Amino terminal propeptide of type I procollagen and osteocalcin; or

(2) Bone specific alkaliphosphatase and osteocalcin.

14. (Previously Amended) The method according to claim 8, wherein the marker that reflects the action of osteoclasts is a marker associated with bone type I collagen.

15. (Previously Amended) The method according to claim 8, wherein the marker that reflects the action of osteoclasts is deoxypyridinoline and/or Carboxyterminal telopeptide of type I collagen.

16. (Currently Amended) The method according to claim 8, <u>wherein there is used:</u>

<u>1) the ratio of A/B in which A is a marker associated with osteoblast calcification and B is a marker associated with osteoblast proliferation or a marker associated with matrix formation, and a marker associated with bone type I collagen, or</u>

2) a ratio of A/B in which A is a marker associated with osteoblast calcification and B is the measured value of a marker associated with osteoblast matrix formation, and the measured value of a marker associated with bone type I collagen.

~~based on the value of a crossover index which is the ratio between a marker associated with the phase of calcification and a marker associated with the phase of osteoblast proliferation and matrix formation and the measured value of the marker that reflects the action of osteoblasts, or on the value of a crossover index which is the ratio between a marker associated with the phase of calcification and a marker associated with the phase of matrix maturation and the measured value of a marker associated with bone type I collagen.~~

17. (Currently Amended) The method according to claim 8~~16~~, wherein there is used:

1) a ratio of A/B in which A is osteocalcin and B is

~~which is based on the value of a crossover index between osteocalcin and~~ Carboxyterminal propeptide of type I pro-collagen or Amino terminal propeptide of type I procollagen and ~~the measured value of~~ Carboxyterminal telopeptide of type I collagen, or

2) a ratio of A/B in which A is osteocalcin and B is

~~on the value of a crossover index between osteocalcin and~~ Bone specific alkaliphosphatase and ~~the measured value of~~ Carboxyterminal telopeptide of type I collagen.

18. (Cancelled)

19. (New) The method according to claim 16, wherein the ratio of A/B is a Z value of an A to Z value of B in which said Z value is:

(an average of measured values for patients with bone metastasis)/(a standard deviation of a patient without bone metastasis).

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20. (New) The method according to claim 6, wherein there is used:

1) a ratio of A/B in which A is a marker associated with osteoblast calcification and B is a marker associated with osteoblast proliferation of a marker associated with matrix formation, and a marker associated with bone type I collagen, or

2) a ratio of A/B in which A is a marker associated with osteoblast calcification and B is the measured value of a marker associated with osteoblast matrix formation, and the measured value of a marker associated with bone type I collagen.

21. (New) The method according to claim 6, wherein there is used:

1) a ratio of A/B in which A is osteocalcin and B is carboxy-terminal propeptide of type I procollagen or amino-terminal propeptide of type I procollagen, and carboxy-terminal telopeptide of type I collagen, or

2) a ratio of A/B in which A is osteocalcin and B is bone-specific alkaline phosphatase, and carboxy-terminal telopeptide of type I collagen.

22. (New) The method according to claim 20, wherein the ratio of A/B is a Z value of an A to Z value of B in which said Z value is:

(an average of measured values for patients with bone metastasis)/(a standard deviation of a patient without bone metastasis).

23. (New) The method according to claim 17, wherein the ratio of A/B is a Z value of an A to Z value of B in which said Z value is:

(an average of measured values for patients with bone metastasis)/(a standard deviation of a patient without bone metastasis).

24. (New) The method according to claim 21, wherein

the ratio of A/B is a Z value of an A to Z value of B in which said Z value is:

(an average of measured values for patients with bone metastasis)/ (a standard deviation of a patient without bone metastasis).